

## Microbial Toxins in E-Liquid: A Potential New Vaping-Related Exposure to Explore

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A new study adds another category of potential harm to the growing list of potentially hazardous vaping-related exposures: organic contaminants of bacterial and fungal origin. The study, published in *Environmental Health Perspectives*,<sup>1</sup> found two markers of microbial contamination in the e-liquid contents of disposable cartridges from first-generation e-cigarettes (or “cigalikes”) and in refill e-liquids.

The researchers took samples from the e-liquid products with the highest listed nicotine content sold by the 10 top-selling U.S. brands, based on 2013 market research data. They tested 2–19 samples from each of the 10 brands, for a total of 75 samples (37 cartridges, 38 refill e-liquids). The team was searching for endotoxin (or lipopolysaccharide), part of the outer membrane of Gram-negative bacteria,<sup>2</sup> and for (1 → 3)- $\beta$ -D-glucan, a common fungal cell wall component. Other studies have found evidence that exposure to either toxin via tobacco smoking may cause adverse health effects.<sup>3</sup>

Their results showed endotoxin levels above the limit of detection (LOD) in 23% of samples; 81% were above the LOD for glucan. The observed glucan concentrations were more than 3 times higher in cartridge than refill samples and significantly higher in tobacco- and menthol-flavored than in fruit-flavored products. For endotoxins, these comparisons were limited by the small number of samples above the LOD.

“The levels [of toxins] we found are fairly low, relative to occupational exposures and even tobacco leaves in traditional

cigarettes,” says senior author David Christiani, who is Elkan Blout Professor of Environmental Genetics at Harvard T.H. Chan School of Public Health. “But if it turns out that these toxins remain intact as aerosols, inhaling low levels at high frequency over a long period of time would generate cumulative exposures that might pose a human health threat.”

According to Christiani, the main sources of endotoxin exposure are agricultural products with close soil contact, such as cotton, grain, hemp, and tobacco. Long-term exposure, which can also affect workers in the livestock and dairy industries, has been associated with chronic lung impairment, asthma, and similar conditions.<sup>4,5,6,7</sup> Christiani has studied endotoxin in a large cohort of Chinese cotton textile workers since 1981.<sup>8</sup>

The toxin (1 → 3)- $\beta$ -D-glucan is a polymer of glucose in the cell walls of most fungi, plants, certain bacteria, and algae.<sup>9</sup> As an indicator of human fungal exposure in indoor environments,<sup>10</sup> it has been associated with atopic asthma and reduced lung function.<sup>10,11</sup>

Because e-cigarette producers do not disclose the sources of materials in their manufacturing pipeline, researchers can only speculate about the reasons for the observed microbial contamination. Possible sources include the cotton wicks in cartridges, tobacco leaves as the origin of natural nicotine, storage containers for the e-liquids, and the raw materials for producing synthetic nicotine and flavoring chemicals. Nonsterile manufacturing conditions may compound the problem.



Endotoxin and (1 → 3)- $\beta$ -D-glucan are both known respiratory irritants. A new study in *EHP* was not designed to assess health effects of inhaling these toxins during e-cigarette use. However, the findings raise the possibility that frequent vaping over a long period could result in potentially harmful cumulative exposures. Image: © Vaper City.

“This pilot study is a great starting point,” says Terry Gordon, a professor of environmental medicine at New York University School of Medicine, who was not involved in the project. “The key question we need to answer next is whether the toxin concentrations are high enough to be of concern when inhaled as aerosols.”

Ana María Rule, an assistant professor of environmental health and engineering at Johns Hopkins University, who also was not involved in the study, agrees that an aerosol analysis is the logical next step. Validating the reported higher prevalence of fungal contamination will be of particular interest, she notes.

“We should also keep in mind that the susceptibility to microbial toxins varies greatly between individuals,” Rule says. “That makes it more challenging for federal agencies to set health standards, but it also means that even low levels of toxins may affect sensitive groups of e-cigarette users.”

Christiani says his team is currently measuring both toxins in aerosols and is including JUUL® brand e-cigarettes in this follow-up analysis. JUUL® products, which have come to dominate the current U.S. market since their 2015 debut, use a novel e-liquid formula to deliver a greater amount of nicotine.<sup>12</sup> Previously identified chemicals of concern in e-cigarettes include vaporized organic chemicals, such as formaldehyde and other aldehydes,<sup>13,14,15</sup> diacetyl and other flavoring chemicals,<sup>16</sup> and toxic metals transferred from the heating coil to the aerosols.<sup>17,18</sup>

Christiani acknowledges that e-cigarettes may be a useful smoking cessation tool for some adults who are struggling with long-term nicotine addiction. However, he is concerned about the rapid uptake of e-cigarettes by young people who otherwise might have avoided tobacco products.<sup>19</sup>

“Buyer beware: If you don’t vape, don’t start,” he says. “E-cigarettes generate a complex exposure cocktail whose [potential] health impact we’re only beginning to understand.”

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